Hausmann, M. (2020). Sex/gender differences in brain activity – It's time for a biopsychosocial approach to cognitive neuroscience. Cognitive Neuroscience, in press.
https://doi.org/10.1080/17588928.2020.1853087

Sex/gender differences in brain activity –

It's time for a biopsychosocial approach to cognitive neuroscience

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Declarations of interest: none

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Abstract

There is compelling evidence that men and women differ in brain activity in long-term memory and other cognitive functions. However, until the origins of sex/gender differences in brain activity, and consequently behaviour, are not fully understood, the factor sex/gender should be considered as imperfect proxy of a combination of yet unknown biological and psychosocial factors underlying these sex/gender differences. The key avenue to a full understanding of sex/gender differences in brain and behaviour depends largely on cognitive neuroscience investigating sex/gender differences in brain activity within a biopsychosocial approach.

The review and meta-analysis by Spets and Slotnick (2020) presents compelling fMRI evidence for sex/gender[1] differences in brain activity during long-term memory. Although the authors focus on long-term memory, sex/gender differences in brain activity have been reported for many other cognitive functions too (e.g., Shaywitz et al., 1995; Hjelmervik et al., 2015), and were even observed in resting-state networks (e.g., Hjelmervik et al., 2014; Weis et al., 2019). However, the direction and degree of these sex/gender differences vary significantly across studies, suggesting that additional factors play an important role. Spets and Slotnick (2020) discuss some confounding factors, such as stimulus type, sample size, direct/indirect statistical comparisons, contrast selection to isolate the cognitive process of interest, etc. However, previous research has shown that intra- and interindividual factors accounting for some of the observed sex/gender differences in brain activities are also highly relevant, and therefore these factors could have received more attention.

As Spets and Slotnick point out, none of the studies included in the meta-analysis used hormonal assays and took hormonal differences between men and women into account, including those related to sex hormonal variations within sexes such as hormonal fluctuations during the menstrual cycle in women. This is surprising because sex hormonal effects on various brain functions and structures are well established in animals (e.g., Woolley & McEwen, 1993, McEwen & Milner, 2017) and humans (e.g., Hausmann, 2017; Hirnstein et al., 2019), suggesting that sex hormones contribute at least to some extent to sex/gender differences in brain and behaviour, although the exact underlying mechanisms are not fully understood.

The decrease in sex/gender differences during long-term memory with increasing age, as reported by Spets and Slotnick (2020), could provide some indirect evidence of hormonal

[1] The terms sex and gender are often used interchangeably in the academic literature, although they refer to different concepts. Sex is primarily used to categorise individuals as either male or female, based on the characteristics of their reproductive system, whereas gender is typically used to refer to social factors related to an individual's sex, or to the individual's personal identification of their gender. In line with a number of recent suggestions (Jäncke, 2018; Joel et al., 2015), I will use the term sex/gender throughout this commentary as since it is not always clear whether results to date are related to sex, gender, or both.

influences. Similar age-related reductions of sex/gender differences in brain and behaviour have been linked to age-related decline in sex hormone levels before, for example in studies investigating postmenopausal women (e.g., Bayer & Hausmann, 2011). However, although sex hormones (i.e., testosterone, oestradiol, progesterone and their metabolites) are known to affect functional brain organisation not only during early ontogenesis (e.g., Beking et al., 2018) but also across lifespan (e.g., Hausmann, 2017), the view that all established sex/gender differences can be completely explained by the action of sex hormones (e.g., oestrogen) is a misconception (Cahill, 2006).

Sex/gender differences in brain activity are often misinterpreted as innate, and it is only recently that neuroscientists have begun to move away from the conception of sex/gender differences as being 'hard-wired' (Jäncke, 2018), and a few recent studies also take into account the influence of social and environmental factors which are known frequently to underlie sex/gender differences in brain and behaviour, such as individual learning experiences and gender stereotypes (Halpern, 2013; Jäncke, 2018). Of particular interest here are studies investigating the complex interaction between biological and psychosocial factors. For example, it has been shown that cognitive sex/gender differences only occurred when gender stereotypes were made salient before cognitive testing, and that testosterone levels in gender-stereotyped men were 60% higher than those of male controls (Hausmann et al., 2009).

Overall, these findings suggest that the factor sex/gender "should be viewed as an imperfect, temporary proxy for yet unknown [biological] factors, such as sex hormones and sex-linked genes" (Maney, 2016, p. 1), and also several non-biological factors. The origins of sex/gender differences in brain activity, and consequently behaviour, are still not fully understood, but they appear to arise from a complex interaction of biological, social, and psychological factors (Halpern, 2000). Surprisingly, little is known about this complex interaction and the multidimensionality of sex/gender differences has not been investigated

much in cognitive neuroscience. However, our understanding of sex/gender differences in brain and behaviour will only improve significantly if more cognitive neuroscientists investigate sex/gender differences in brain activity within a biopsychosocial approach.

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